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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,768	06/19/2001	Mark A. Exley	01948/074002	4022

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EXAMINER	
JALLA, SANJOO	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,768	EXLEY ET AL.	
	Examiner	Art Unit	
	Sanjoo Shree Jalla	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-68* is/are pending in the application.

4a) Of the above claim(s) *6,8-42 and 45-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-5, 7, 43-44 and 52-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 12/30/05, is acknowledged.

   Claims 1, 3-5, 7, 9-11, 23, 27, 29, 31, 33, 35 have been amended.
   Claims 43-68 have been added.
   Claims 1-68 are pending.

   Applicant's election with traverse of group I (claims 1-5 and 7), drawn to a purified antibody, a hybridoma that produces an antibody and a combination of purified antibodies that preferentially binds a CDR3-loop of T cell antigen receptor (TCR), in the reply filed on 12/30/05 is acknowledged. The traversal is on the grounds that it would not be an undue burden to examine the antibody of group I along with a method of generating the antibody comprising immunizing a mammal with coupled peptides of group X and a method of generating and isolating an antibody, comprising immunizing a CD1 or invariant T cell deficient mammal with invariant T cells of group XIII and a method of increasing the size of a subpopulation of T cells, comprising contacting said T cells with an antibody or a combination of antibodies of group XLVI and a method of increasing the size of a subpopulation of T cells, comprising contacting T cells with an antibody or a combination of antibodies conducted under conditions that allow complex formation between said T cells and said body in the presence or absence of alpha-galactosylceramide antigen of group XLIX. This is not found to be persuasive because antibody, which is a product, is patentably distinct from a method of making the antibody and a method of using it. In addition, antibodies and related methods are recognized divergent subject matter, as exemplified by their different classifications. Therefore these products and methods are distinct and independent, and searches for both would place an undue burden upon the examiner. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention.

   The requirement is still deemed proper and is therefore made FINAL.

   Claims 1-5, 7, 43-44 and 52-68 read on the elected invention and are being acted upon.

   Claims 6, 8-42 and 45-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

   Therefore, claims 1-5, 7, 43-44 and 52-68 are under consideration in the instant application.

2. The oath or declaration is defective because, it does not identify the citizenship of inventor Mark Exley.

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, e.g. on page 24. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4. The title of the invention is not descriptive. Applicant should restrict the title to the claimed invention. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. The abstract of the disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP § 608.01(b).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.*

Claims 53 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The term "modulate" in claims 53 and 65 is indefinite because it is not clear what sort of activity is encompassed by the term. The term modulate could be interpreted in different ways. For example, modulate could indicate that the T cells are being proliferated, or it could also indicate that cells are up regulated or down regulated to an unspecified degree. Since the term is not defined in the specification it is not clear what "modulating" encompasses. Modulate also might encompass fast/slow, on/off, up/down activity. Further, it is not clear what degree, direction, or type of modulation is required for the claimed invention to function as a method of cell expansion or activation. One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

b) Claims 43 and 44 are indefinite in that they recite 6B11 or 3A6 as an arbitrary antibody name. Claims do not distinctly recite a specific antibody. Applicant should particularly point out and distinctly recite "6B11 or 3A6" antibody by claiming characteristics associated with the antibody (e.g. amino acid sequence). Claiming biochemical molecules by a particular name given to the antibody by various workers in the field fails to distinctly claim what that antibody is and of what the compositions it is made. One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

c) Claims 64-68 are indefinite in that they recite "antibody". The claims do not distinctly recite a specific antibody. Applicant should particularly point out and distinctly recite "said antibody" by claiming characteristics associated with the antibody (e.g. amino acid

sequence). One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

d) Claims 1-5, 7, 43-44, 52-68 are indefinite in that they recite "CDR3 loop". Given the definition of the specification, it cannot be determined the CDR3-loop begins or ends. One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

e) Claims 43-44 are indefinite in that they recite antibody and hybridoma by same name i.e. 6B11 or 3A6. Antibody and hybridoma cannot have same name. One could say for example, antibody produced by 6B11 or 3A6, or hybridoma that produces the 6B11 or 3A6 antibody. One of ordinary skill in the art would not be reasonably able to establish the metes and bounds of the claimed invention.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

Claims 60 and 61 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

Applicant should specifically point out the support for any amendments made to the claims. See MPEP 2163.06.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) The fragment or derivative of an antibody of claim 5, wherein said antibody is a monoclonal antibody (claim 60).
B) The fragment or derivative of an antibody of claim 5, wherein said fragment or derivative is humanized (claim 61).

A review of the specification fails to reveal support for the new limitations.

Regarding A) and B), the specification (pages 7 and 8) discloses an antibody to be a monoclonal antibody and to be humanized but the specification as filed does not appear to provide a written description for the limitation of claims 60 and 61, where the fragment or derivative of an antibody is a monoclonal antibody and is humanized.

8. Claims 4-5 and 57-63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant has disclosed "a fragment or derivative thereof" (Claims 5 and 57-63). The skilled artisan cannot envision what exactly the applicant means by "a fragment or derivative thereof", in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features that are common to the genus. That is, the specification does not provide a representative number of species and description of structural features that are common to species, to describe the claimed genus (a fragment or derivative thereof). Specification does not disclose any fragment or derivative of an antibody (species), encompassed by the claims. The genus of "a fragment or derivative thereof" is large as it would encompass Fab, F(ab')2, Fd, single-chain Fvs (scFv), a fragment that consists of Fc portion only or conceivably even 2 amino acid fragments. Given the size of the claimed genus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus (a fragment or derivative thereof).

9. Claims 43 and 44 are rejected under 35 U.S.C. 112, first paragraph, as containing

subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the **hybridoma that produce the** 6B11 or 3A6 **antibody** is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the **hybridoma**, which produces this antibody, may satisfy first paragraph. See 37 CFR 1.801-1.809.

If the deposit(s) ha(ve)s been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the **hybridoma** has been deposited under the Budapest Treaty and that the **hybridoma** will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample *or for the enforceable life of the patent whichever is longer.* See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

If the deposit(s) was/were made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the **hybridoma** described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Further, amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required as set forth in 37 C.F.R. 1.809(d). As an additional means for completing the record, Applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

NOTE THE CURRENT ATCC DEPOSITORY ADDRESS:
American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209

If the original deposit is made after the effective filing date of an application for patent, Applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state that the biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which case the statement need not be verified. See 37 CFR 1.804(b) and MPEP 2406.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> *(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

Claims 1, 3, 7, 55 and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Jameson et. al. (The Journal of Immunology. 1991; 147: 3185-3193) as evidenced by Janeway et. al. (Immunobiology, Current Biology Limited. 3rd Edition. 1997, page 4:36).

Jameson et. al. teach an antibody (monoclonal) that recognizes V alpha11 family haplotypes with J-alpha dependency (see in particular abstract) i.e. an antibody to CDR3 loop of TCR because as evidenced by Janeway et. al. D-, J- and N-nucleotide encodes the CDR3 loops in T cell receptors that form the center of the antigen binding site (see in particular page 4:36). Further, since the antibody is a monoclonal antibody, it is a purified antibody. Further, CDR region of the TCR is an antigen-binding site so if the antibody binds to CDR region it binds to antigen binding site of the TCR.

The reference clearly anticipates the invention

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

Claims 1-3, 7, 52-54, 64-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Exley et. al. (J. Exp. Med. 1997; 186: 109-120) in view of Campbell (ed.), Monoclonal Antibody Technology, 1985; 2nd Edition.

Exley et. al. teach an invariant Vα24-JαQ TCR-α amino acid sequence (i.e.CDR3 loop of TCR) (see in particular Figure 1.).

Exley et. al. do not teach an antibody that binds a CDR3-loop of TCR.

Campbell teaches that it is customary for any group working on protein to make monoclonal antibodies from hybridoma to it (see Chapter 1, page 29, last paragraph). Further, Campbell teaches that monoclonal antibodies are useful for therapeutic, diagnostic, preparative and basic research purposes (pp 20).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Campbell to make an antibody to the invariant Vα24-JαQ TCR-α amino acid sequence (i.e.CDR3 loop of TCR) as taught by Exley et. al.

One of ordinary skill in the art at the time the invention was made would have been motivated to make antibodies (monoclonal) against the invariant Vα24-JαQ TCR-α amino acid sequence (i.e.CDR3 loop of TCR) as taught by Exley et. al. because it is routine to study a protein's properties or biological functions and to do so, making an antibody would be the first step. Further, since the invariant Vα24-JαQ TCR-α amino acid sequence (i.e.CDR3 loop of TCR) as taught by Exley et. al. is identical to the human sequence of the CDR3 loop taught by the specification (page 52), antibody binding to invariant Vα24-JαQ TCR-α amino acid sequence (i.e.CDR3 loop of TCR) of Exley et. al. would also result in expansion of an invariant T cell and modulation of expansion or activation of T cell population.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

12. Claims 5, 56-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Exley et. al. (J. Exp. Med. 1997; 186: 109-120) and Campbell (ed.), Monoclonal Antibody Technology, 1985; 2nd Edition as applied to claims 1-3, 7, 52-54, 64-68 in view of Gavilondo et. al. (Antibody engineering at the Millennium. Biotechniques. 2000; 29: 128-145).

The teachings of Exley et. al. and Campbell have been discussed previously.

Exley et. al. and Campbell do not teach a fragment wherein the fragment is a ScFv, Fab, or $F(ab)_2$ fragment or derivative of an antibody that binds a CDR3-loop of a TCR. Exley et. al. and Campbell further do not teach antibody or fragment of the antibody to be humanized.

Gavilondo et.al. teach that it is well known in the art at the time the invention was made to prepare antibody fragments, or single chain antibodies i.e. Fab, $F(ab')_2$ and Fv fragment (see Table 1, page 130 in particular) or , humanized antibodies. Further Gavilondo et.al. teach that antibody fragments and humanized antibodies are useful for

a number of procedures including detection assays as well as diagnostic and therapeutic regimens because of their smaller size and potentially better tissue penetration and clearance (see page 132, left column-second paragraph, lines 7-12).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make fragments of antibody i.e. Fab, F $(ab')_2$ and Fv that is humanized as taught by Gavilondo et.al. to the antibody as taught by the Exley et. al. and Campbell for use in detoxification of drugs and toxins and diagnostic assays.

The ordinary artisan at the time the invention was made would have been motivated to produce humanized antibodies and fragments of antibody i.e. Fab, F $(ab')_2$ and Fv as taught by Gavilondo et.al. to the antibody as taught by Exley et. al. and Campbell because antibody fragments and humanized antibodies have potential advantages over whole antibodies for many therapeutic uses because of their smaller size and potentially better tissue penetration and clearance as taught by Gavilondo et.al. (see page 132, left hand column, and lines 10-15 in particular).

From the teachings of the references, it was apparent that one of ordinary skill in the art would have a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

13. Claim 63 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jameson et. al. (The Journal of Immunology. 1991; 147: 3185-3193) and Janeway et. al. (Immunobiology, Current Biology Limited. 3rd Edition. 1997, page 4:36) as applied to 1, 3, 7, 55 and 68 claims and in further view of Harlow et.al. (Antibodies A Laboratory Manual, Cold Spring Harbor Press, 1988).

The teachings of Jameson et. al. and Janeway et. al. have been discussed previously.

Jameson et. al. and Janeway et. al. do not teach an antibody coupled to a detectable substance.

Harlow et.al. teach that labeling antibodies with an easily detectable "tag" can be used to identify specific antigens even when displayed in a complicated mixture of other molecules (see content page vi-Labeling Antibodies in particular). Further, Harlow et.al. teach that labeled antibodies can be used in techniques like immunoassays, immunoblots, immunohistochemistry etc. (see Table 9.1, page 322 in particular). Harlow et.al. further teach that labeled antibodies are extremely useful detection tools in immunological techniques (see page 321, lines 1-2 in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make a detectably labeled antibody as taught by Harlow et.al. to

the antibody as taught by Jameson et. al. and Janeway et. al. for use in immunoassays, immunoblots, immunohistochemistry etc. (see Table 9.1, page 322 in particular).
The ordinary artisan at the time the invention was made would have been motivated to produce labeled antibodies as taught by Harlow et.al. to the antibody fragment as taught by Jameson et. al. and Janeway et. al. because labeled antibodies are extremely useful detection tools in immunological techniques as taught by Harlow et.al. (See page 321, lines 1-2 in particular).

From the teachings of the references, it was apparent that one of ordinary skill in the art would have a reasonable expectation of success in arriving at the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sanjoo Jalla whose telephone number is (571) 272-4453. The examiner can normally be reached Monday through Friday from 8:00 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

16. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sanjoo Jalla, Ph.D.
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3/2006

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER